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Review

Cognitive and Perceptual Functions of the Visual Thalamus

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The thalamus is classically viewed as passively relaying information to the cortex. However, there is growing evidence that the thalamus actively regulates information transmission to the cortex and between cortical areas using a variety of mechanisms, including the modulation of response magnitude, firing mode, and synchrony of neurons according to behavioral demands. We discuss how the visual thalamus contributes to attention, awareness, and visually guided actions, to present a general role for the thalamus in perception and cognition.

> The [cortex] must depend entirely on the thalamus for the precise nature of the sensory material which it receives indirectly from peripheral receptors. It is true that there is evidence to indicate that cortical mechanisms can modify thalamic activities by inhibitory influences, but the fact remains that […] the [cortex] from the developmental and functional point of view is to be regarded as a dependency of the thalamus and not vice versa. (Le Gros Clark, 1932, p. 406)

Introduction

Galen (129–199/217 AD) was the first to call the mass of nuclei that constitute the diencephalon *thalamos*, a Greek word meaning inner room or chamber (Jones, 2007). Deep within the brain, the thalamus and surrounding cortex form a closely coupled system: the thalamus transmits information from the environment and internal processes to the cortex, while the cortex sends the output from multiple processing stages to the thalamus. The cortex critically depends on the thalamus, since it receives relatively little other input.

The thalamus has been extensively studied in terms of its anatomical organization, efferent and afferent connectivity patterns, basic neural response properties, and synaptic, biochemical, and molecular characteristics (Jones, 2007; Sherman and Guillery, 2006). However, its role in perception and cognition has remained poorly understood. Studies in awake, behaving monkeys during the last decades have focused almost exclusively on defining the roles of cortical areas in attention, memory, decision making, and other cognitive processes. Similarly, human neuroimaging studies have heavily emphasized the functions of cortical rather than subcortical networks, partially due to technical limitations in terms of spatial resolution. During the last few years, we have seen the beginning of a renaissance for the study of thalamic function in perception and cognition due to the development of functional magnetic resonance imaging (fMRI) at high resolution that permitted for the first time the study of the human thalamus in some detail (reviewed in Saalmann and Kastner, 2009), followed by a renewed interest of physiologists in thalamic function in awake, behaving monkeys (e.g., McAlonan et al., 2006, 2008). In the present review, we will focus on the visual thalamus as a model system to exemplify the changing views of the thalamus's role in perception and cognition that have begun to emerge from these studies.

The visual thalamus consists of three main nuclei, the lateral geniculate nucleus (LGN), the thalamic reticular nucleus (TRN), and the pulvinar. These three structures are characterized by differences in their efferent and afferent connectivity patterns (Jones, 2007; Sherman and Guillery, 2006). The LGN is considered a first-order thalamic nucleus because it transmits peripheral signals to the cortex, along the retino-cortical pathway. In addition to retinal afferents that form only a minority of the input to the LGN, it receives projections from multiple sources including primary visual cortex (V1), the TRN, and brainstem. Thus, the LGN represents the first stage in the visual pathway at which modulatory influences from other sources could affect information processing. The TRN forms a thin shell of neurons that covers the lateral and anterior surface of the dorsal thalamus, and it receives input from branches of both thalamo-cortical and cortico-thalamic fibers. The TRN in turn sends its output exclusively to the thalamus and is positioned to provide inhibitory control over thalamo-cortical transmission. The pulvinar is the largest nucleus in the primate thalamus and is considered a higher-order thalamic nucleus because it forms input-output loops almost exclusively with the cortex. The extensive and reciprocal connectivity with the cortex suggests that the pulvinar serves in aiding cortico-cortical transmission through thalamic loops. Thus, from an anatomical perspective, the visual thalamus is ideally positioned to regulate the transmission of information to the cortex and between cortical areas, as was originally proposed more than 20 years ago (Crick, 1984; Sherman and Koch, 1986; Singer, 1977). The experimental evidence in favor of such a functional role will be reviewed in the following sections, which are organized by thalamic nucleus.

LGN: Early Modulation of Visual Information

In the case of the LGN, the classical view of the thalamus as a passive relay of information from the sensory periphery to

cortex may have been largely based on the high specificity of retinal afferents to the LGN and the similarity of receptive field (RF) properties of retinal ganglion cells and LGN neurons. However, by the early 1980s, evidence was emerging that thalamic neurons operate in one of two modes, either burst or tonic firing of action potentials (Deschênes et al., 1982; Llinás and Jahnsen, 1982; Mukhametov et al., 1970). These two firing modes suggested that thalamic neurons were not simple relays, but instead were in a position to differentially transmit retinal information to visual cortex. By the mid- to late 1980s, theoretical accounts proposed active roles for the thalamus in regulating information transfer to the cortex (Crick, 1984; Sherman and Koch, 1986; Singer, 1977), but further evidence in support of such roles was not immediately forthcoming. Instead, burst firing was shown to be common during sleep (Livingstone and Hubel, 1981; Steriade et al., 1993) and thus a possible role for bursts during wakefulness was not apparent. Moreover, cognitive influences such as selective attention appeared to affect neural responses only in visual cortex, but not in the LGN, where little, if any, modulation was found in early studies (Bender and Youakim, 2001; Lehky and Maunsell, 1996; Mehta et al., 2000). Consequently, this evidence led to a notion that perceptual and cognitive influences may affect neural processing only at the cortical level. This account has been revised during the last few years based on reports of attentional and perceptual modulation in the human and macaque LGN (e.g., McAlonan et al., 2008; O'Connor et al., 2002).

Anatomy and Physiology

LGN topography and the response properties of LGN neurons have been extensively studied in anesthetized nonhuman primates (e.g., Connolly and Van Essen, 1984; Kaas et al., 1972; Malpeli and Baker, 1975). The LGN is typically organized into six main layers, and each layer receives input from either the contra- or the ipsilateral eye. The four dorsal layers contain small (parvocellular) neurons that are characterized by sustained discharge patterns and low contrast sensitivity, largely processing form and color information. The two ventral layers contain large (magnocellular) neurons that are characterized by transient discharge patterns and high contrast sensitivity, largely processing motion and depth information (Creutzfeldt et al., 1979; Derrington and Lennie, 1984; Dreher et al., 1976; Merigan and Maunsell, 1993; Shapley et al., 1981; Wiesel and Hubel, 1966). In addition, there are six thin LGN layers, located ventral to each of the parvo- and magnocellular layers, that contain very small (koniocellular) neurons, some of which carry signals from short-wavelength-sensitive (blue) cones (Hendry and Reid, 2000; Martin et al., 1997; Roy et al., 2009; Xu et al., 2001). These three LGN cell classes target different cortical layers (Figure 1A). Parvocellular and magnocellular neurons project to layer 4 and to a lesser extent to layer 6, while koniocellular cells project to layers 1 and 3 of area V1 and to extrastriate areas as well (reviewed in Callaway, 2005).

Each LGN contains a retinotopic map of the contralateral visual hemifield. Similar to retinal ganglion cells, LGN cells have circular RFs, typically with an antagonistic center-surround organization. Despite the similarities in response characteristics between retinal ganglion and LGN cells, there are a number of signal transformations that occur across retino-geniculate

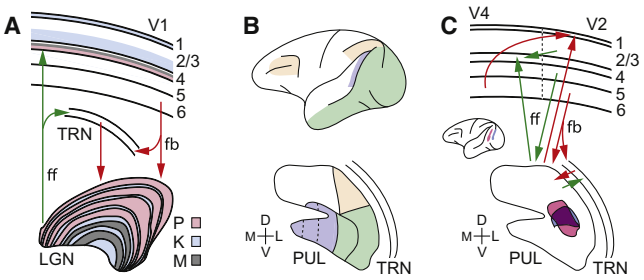

Figure 1. Thalamo-Cortical Connectivity

(A) Feedforward (ff) projections from parvo-, konio-, and magnocellular (P, K, M) neurons in the LGN target specific layers in V1 (color-coded). Layer 6 feedback (fb) from V1, respectively, targets P, K, and M layers of the LGN.

(B) Fronto-parietal (yellow), medio-temporal (violet), and infero-temporal and occipital (green) cortical regions preferentially connect with different divisions of the pulvinar (PUL). The ventro-lateral and ventro-central divisions shown in green are retinotopically organized. Note that there are alternative parcellation schemes of the pulvinar based on neurochemical criteria (Gutierrez et al., 1995; Stepniewska and Kaas, 1997; Adams et al., 2000); however, there is reasonable agreement on subdivisions of the ventro-medial pulvinar (dotted lines).

(C) Direct cortico-cortical connections (top) and indirect cortico-pulvino-cortical loops exemplified by V2-pulvino-V4 circuitry. Tracer injections into V2 (blue) and V4 (pink; inset) showed overlapping (purple) projection zones in the pulvinar (bottom). Adapted with permission from Figure 8 in Adams et al. (2000).

synapses. For example, retinal action potentials following a short interspike interval are more likely to generate action potentials in LGN neurons than those following longer intervals. These relayed spikes are more highly correlated with the visual stimulus—that is, they have greater spike timing precision than nonrelayed spikes. Consequently, relayed spikes carry more visual information per spike, enabling LGN neurons to improve coding efficiency (Rathbun et al., 2010; Wang et al., 2010b).

In the human LGN, the layout of the visual field representation was initially studied using postmortem anatomical analyses of degeneration patterns following retinal and cortical lesions (e.g., Hickey and Guillery, 1979). This layout was later confirmed in detail using high-resolution fMRI techniques (Figure 2A; (Schneider et al., 2004), revealing a close correspondence between the topographies of the macaque and human LGNs. Anatomical studies have also revealed laminar patterns of parvo- and magnocellular subdivisions similar to the macaque LGN (Hickey and Guillery, 1979). Although current neuroimaging techniques are insufficient to resolve single lamina within the human LGN, magno- and parvocellular-dominated regions of the LGN can be identified based on functional criteria—that is, the higher contrast sensitivity of magno- relative to parvocellular neurons (Derrington and Lennie, 1984; Sclar et al., 1990). Hence, it is possible to probe how magno- and parvocellular processing contributes to human behavior and cognition, since the LGN is the only structure in the visual system where the two pathways are sufficiently spatially segregated to be resolved using current fMRI methods.

In addition to retinal afferents, the LGN receives modulatory input from multiple sources. Cortico-thalamic feedback projections from V1 comprise about 30% of the input to the LGN, and inhibitory input from the TRN and local interneurons contributes another 30% of LGN input (Sherman and Guillery, 2006).

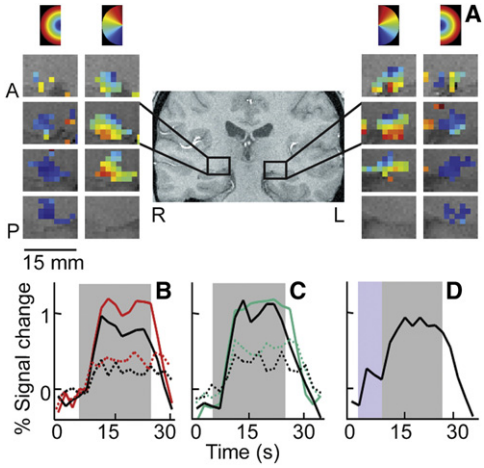

Figure 2. Attentional Modulation of Human LGN Responses

(A) Retinotopic organization of the LGN for a representative subject. Polar angle and eccentricity maps are shown in columns of sequential slices from anterior (A) to posterior (P), for the right (R) and left (L) LGN. The color code at the top of columns shows regions of the visual field to which LGN voxels preferentially responded.

(B–D) Time series of fMRI signals in the LGN averaged across subjects (n = 4) and hemispheres. Gray area shows period of checkerboard stimulus presentation. (B) Directed attention (red lines) enhanced responses to high (solid) and low (dashed) contrast stimuli, relative to the unattended condition (black lines). (C) Responses to high (solid) and low (dashed) contrast stimuli were suppressed during a fixation task of high attentional load (black lines) relative to a low-load fixation task (green lines). (D) Attention directed to the periphery in expectation (blue area) of the visual stimulus increased baseline activity. (A) is reprinted with permission from Figure 2 in Schneider et al. (2004); (B)–(D) are reprinted with permission from Figure 2 in O'Connor et al. (2002).

Both V1 and TRN represent visual information in retinotopically organized maps and can thereby influence LGN responses in spatially specific ways. Moreover, V1 feedback arises from three classes of neurons, each selectively targeting parvo-, magno- or koniocellular LGN neurons (Briggs and Usrey, 2009). This finding suggests that cortico-thalamic feedback may differentially modulate information processing in parvo-, magno-, and koniocellular afferent pathways and thus be more selective than the TRN input to LGN. A third major modulatory influence that represents another 30% of input to the LGN arises from brainstem nuclei—that is, the pedunculopontine tegmentum and the parabigeminal nucleus. These cholinergic projections are more diffusely organized than the V1 and TRN projections (Bickford et al., 2000; Erişir et al., 1997) and, consequently, are likely to influence LGN responses with less spatial specificity. Due to the multiple modulatory inputs, the LGN is well positioned for early regulation of visual information transmission.

Attentional Response Modulation

Human fMRI studies provided the first compelling evidence of cognitive tasks that modulated LGN responses. In a series of attention experiments, O'Connor et al. (2002) showed that selective attention affects visual processing in at least three different ways, similar to the modulatory effects observed in visual cortex. First, LGN responses to attended visual stimuli increased relative to the same stimuli when unattended (Figure 2B). This response enhancement was specific to the attended visual field location and occurred in both parvo- and magnocellular regions of the LGN, although the attentional enhancement tended to be stronger in magnocellular regions (Schneider and Kastner, 2009). Second, neural responses to unattended stimuli were attenuated depending on the load of attentional resources engaged elsewhere (Figure 2C). This is consistent with a deoxyglucose study in macaques showing suppressed metabolic activity peripheral to the attended stimulus representation, largely in magnocellular LGN layers (Vanduffel et al., 2000). Third, baseline activity increased when participants directed attention to a location in the absence of visual stimulation and in anticipation of the upcoming stimulus (Figure 2D). All three attention effects tended to be larger in the LGN than in V1, with effects on the order of the attentional modulation typically observed in extrastriate areas such as V4. Thus, feedback from V1 may only partly contribute to the attentional modulation of LGN responses, suggesting that additional sources such as the TRN and brainstem cholinergic inputs may contribute as well.

The finding of attentional modulation in the human LGN has been corroborated by a recent single-cell recording study in the macaque LGN that provides a more space- and time-resolved view of the attention effects (McAlonan et al., 2008). The spike rate of LGN neurons increased for attended stimuli relative to unattended stimuli, with slightly stronger effects on magnocellular neurons (11% enhancement) than parvocellular neurons (9%; Figures 3A and 3B) across the population. Selective attention also influenced magnocellular neurons earlier than parvocellular neurons (the influence of attention on koniocellular neurons is not known). The attention effects varied over time, as evidenced by an early period of attentional modulation within the first 100 ms after stimulus onset, and a later period of modulation starting around 200 ms, possibly reflecting different sources of modulatory input. Based on the response patterns of TRN and V1 neurons, it is possible that the early period of attentional effects in the LGN is attributable to TRN influences, whereas the late period may reflect feedback from V1 (Figure 1A).

Perceptual Response Modulation

The thalamus may contribute not only to the selection of behaviorally relevant information from the environment, but also to the conscious perception or awareness of visual information. A classical task to probe visual awareness is binocular rivalry, in which dissimilar images such as gratings of orthogonal orientation are presented to the two eyes. This leads to a competition for perceptual dominance where only one image is visible at a time while the other one is suppressed (Figure 4A). Human neuroimaging studies have shown that activity in the LGN reflects the subjects' reported percept and not necessarily the actual retinal input (Haynes et al., 2005; Wunderlich et al., 2005). For example, while a grating of different contrast and orientation was presented to each eye, LGN activity increased when participants perceived a high-contrast horizontal grating and decreased when they perceived a low-contrast vertical grating, similar to the response pattern that is evoked by physical alternations of the same stimuli (Figure 4B; Wunderlich et al., 2005). However, these findings contrast somewhat with results from macaque physiology studies. Using a generalized flash suppression task, in which a target stimulus is no longer perceived after being surrounded by randomly moving dots, there was no

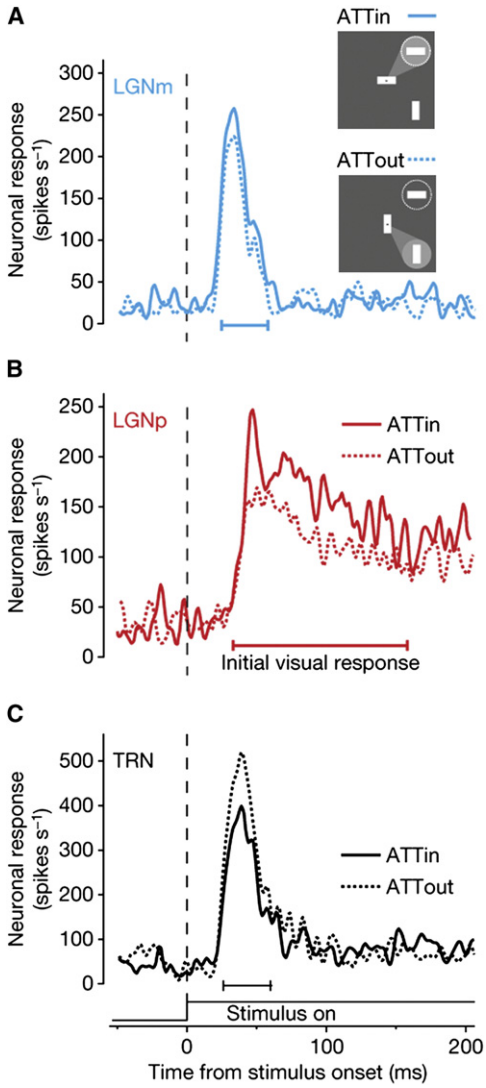

Figure 3. Attention Effects on Macaque LGN and TRN Neurons
(Inset) Monkeys were cued to direct their attention to a visual stimulus inside (ATTin) or outside (ATTout) the receptive field (circle). Selective attention increased spike rates of (A) magno- and (B) parvocellular LGN neurons, but reduced spike rates of (C) TRN neurons. Reprinted with permission from Figure 1 in McAlonan et al. (2008).

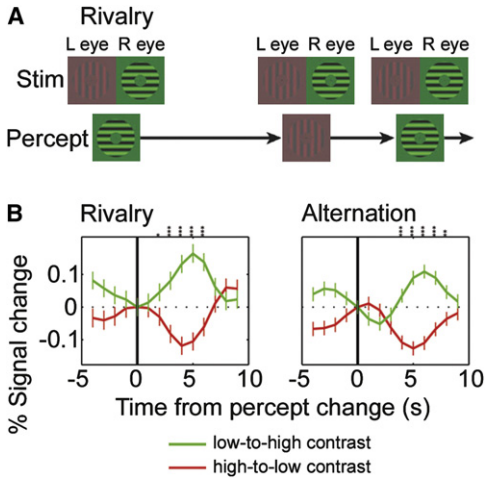

Figure 4. LGN Responses Reflect Perceptual Experience during Binocular Rivalry
(A) Schematic view of the visual stimuli presented to each eye (top row) and the subject's perceptual experience (bottom row) during the binocular rivalry task.
(B) Mean fMRI signal from the LGN for all switches from low-to-high (green) or high-to-low (red) contrast percepts. Data from both hemispheres of all five subjects combined.
(Left) Although the retinal stimulation did not change, LGN responses increased when subjects perceived the high contrast stimulus and decreased when they perceived the low contrast stimulus (manual report of percept at t = 0).
(Right) Physically alternating the visual stimuli (i.e., only presenting the high or low contrast stimulus at any one time) produced a similar pattern of LGN responses. The same response pattern during rivalry and physical alternations was also seen in V1, suggesting that the LGN/V1 circuit resolves the rivalry between simple grating stimuli. Difference between the green and red curves: t test, *p < 0.05; **p < 0.01; ***p < 0.001. Reprinted with permission from Figures 1 and 2 in Wunderlich et al. (2005).

perceptual modulation of the spike rate of macaque LGN neurons (Wilke et al., 2009). Since mainly parvocellular neurons were studied, it is unclear how flash suppression affects magno- and koniocellular neurons. For example, it is possible that perceptual modulation is largely limited to magnocellular neurons, and thus the magnocellular LGN was driving the responses in the human fMRI studies. Another possibility is that changes in response timing and synchrony of LGN neurons contributed to the signal changes observed in the human fMRI studies, thereby raising the question of the type of neural signals that underlie hemodynamic signals measured with fMRI. fMRI signals can be reliably predicted from local field potentials (LFPs), which reflect subthreshold membrane potentials, including synaptic events, oscillatory activity, and after-potentials (Logothetis and Wandell, 2004). Importantly, LGN LFPs reflect, in large part, the modulatory inputs to the LGN and subthreshold oscillatory activity that can influence the spike timing and synchrony of LGN neurons. As further elaborated below, particularly, alpha (8–13 Hz) and beta (14–30 Hz) oscillations have been reported to shape the timing of LGN responses. Interestingly, the flash suppression task modulated LFPs in the LGN in the alpha and beta frequency range. Thus, considering modulation of LGN LFPs and spike timing, rather than spike rate, may reconcile the discrepancy between monkey physiology and human fMRI studies on perceptual modulation. However, it remains to be probed whether reported perceptual dominance or suppression alters the temporal structure of LGN spiking activity.

Burst and Tonic Response Modes

Modulating the response magnitude of LGN neurons is one mechanism by which information transmitted to the cortex can be influenced depending on behavioral context. Switching the response mode of LGN neurons potentially represents another important mechanism to regulate thalamo-cortical transmission. Thalamic neurons respond in one of two modes, tonic or burst firing mode, depending on a calcium current (I_T) through a low threshold calcium channel (T channel). The calcium channel is inactivated when the neuron is depolarized and deinactivated

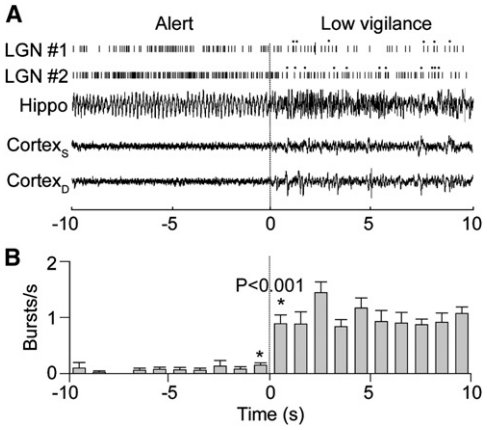

Figure 5. Burst Firing of LGN Neurons Depends on the Level of Vigilance

(A) Burst firing of two spontaneously active LGN neurons increased when the rabbit shifted from an alert (left) to a low-vigilance (right) state. Asterisks denote bursts. EEG recorded from the hippocampus (Hippo) as well as the superficial ($Cortex_S$) and deep ($Cortex_D$) layers of the cortex showed the state change (at t = 0 s).

(B) Mean burst rate of ten spontaneously active LGN neurons before and after the change in vigilance. Reprinted with permission from Figure 5 in Bezdudnaya et al. (2006).

when the neuron is hyperpolarized for at least 50 ms. When the calcium current is inactivated, the neuron responds linearly to its input, with a relatively steady train of action potentials (tonic mode). When the calcium current is activated, the neuron responds to its input in a less linear fashion, with a burst of action potentials (burst mode)—that is, I_T activates a Ca^{2+}-dependent spike, activating a burst of Na^+ spikes (Huguenard, 1996). For example, suppressive stimuli may cause sufficiently prolonged hyperpolarization of an LGN neuron to deinactivate low-threshold calcium channels. A subsequent depolarizing input is then more likely to induce the LGN neuron to burst fire (Alitto et al., 2005; Denning and Reinagel, 2005; Lesica and Stanley, 2004). Because bursts are more efficacious in activating thalamo-cortical synapses than tonic spikes (Swadlow and Gusev, 2001), burst firing mode may be useful for initially detecting stimuli (Fanselow et al., 2001). After stimulus detection, a switch to tonic firing mode would allow thalamic neurons to be more faithful to their retinal input, reliably transmitting information from retinal afferents to the cortex, for more detailed information processing. Such switching of firing modes has been shown in the cat LGN, in which most bursting occurred during early responses to a visual stimulus, followed by tonic firing (Guido and Weyand, 1995). The degree of vigilance also appears to influence the firing mode of thalamo-cortical neurons. LGN neurons tend to burst more when rabbits were in a low vigilance state than in an alert state, and this switch in firing mode occurred within one second of the EEG-defined state transition (Figure 5; Bezdudnaya et al., 2006). The increased bursting may allow the detection of stimuli that are relevant for ongoing behavior even when in an inattentive state. Importantly, both cortical feedback as well as cholinergic brainstem influences have been shown to depolarize LGN neurons (Scharfman et al., 1990) and thus are able to switch their firing mode from burst to tonic (Lu et al., 1993; McCormick and von Krosigk, 1992; Varela and Sherman, 2007). However, little is known about the way in which cognitive processes may impact the firing mode of thalamic neurons.

Neural Synchrony and Oscillations

Thus far, we have considered influences on response magnitude and firing mode as mechanisms to modulate the efficacy of thalamic drive to the cortex. Synchronizing thalamic output represents yet a third relevant mechanism, which may be particularly effective in light of the reported low efficacy of thalamo-cortical synapses (Bruno and Sakmann, 2006). Accordingly, simultaneous recordings from the LGN and V1 in anesthetized cats have found that correlated spiking of LGN neurons increased their efficacy in driving cortical neurons (Alonso et al., 1996). Neurons with greater overlap of their RFs showed greater synchrony. A recent modeling study estimated that as few as 5 to 10 synchronized LGN cells may be sufficient to drive a cortical neuron (Wang et al., 2010a). Thus, modulating the synchrony of a group of thalamic neurons may be a potent mechanism to regulate information transmission to cortex.

Synchronizing the activity of two groups of neurons can also increase their information exchange (Gregoriou et al., 2009; Saalmann et al., 2007; Tiesinga and Sejnowski, 2009; Womelsdorf et al., 2007). Spikes are more likely to be relayed if those from presynaptic neurons arrive during periods of reduced inhibition of postsynaptic neurons. This spike timing relationship can be achieved by synchronizing oscillatory activity of pre- and postsynaptic neurons with an appropriate phase lag. Consequently, synchrony between thalamic and cortical neurons, with LGN leading, may increase the efficacy of thalamic input to cortex. Consistent with such a gain control mechanism, it has been found that attentive viewing synchronizes beta frequency oscillations of LFPs in cat LGN and V1 (Bekisz and Wróbel, 1993; Wróbel et al., 1994). Such synchrony largely seems to occur between interconnected groups of neurons in each area (Briggs and Usrey, 2007; Steriade et al., 1996), offering the possibility of spatially specific control of information transmission.

LGN synchrony and oscillations are controlled by the areas that provide modulatory inputs to the LGN—that is, V1, TRN, and cholinergic brainstem nuclei. Importantly, these sources may differentially influence different oscillation frequencies (the TRN input is discussed in its own section below). For example, evidence suggests that the cholinergic input to the thalamus regulates alpha oscillations in the LGN, as evidenced by activation of muscarinic cholinergic receptors that induce alpha oscillations of LFPs in the LGN (Lörincz et al., 2008). Thalamo-cortical cell firing appears to be correlated with these alpha oscillations, with different groups of LGN neurons firing at distinct phases of the alpha oscillation (Lorincz et al., 2009). Thus, cholinergic inputs to the LGN may influence thalamo-cortical transmission by changing the synchrony of LGN neurons (Hughes and Crunelli, 2005; Steriade, 2004). Because cholinergic tone increases with vigilance (Datta and Siwek, 2002), cholinergic influence on thalamo-cortical transmission may be modulated by behavioral context. Moreover, the thalamus is critically involved in generating cortical alpha rhythms (Hughes and Crunelli, 2005), which are linked to spatial attention bias and

stimulus visibility (Mathewson et al., 2009; Romei et al., 2010; Thut et al., 2006). In comparison, feedback from V1 may influence alpha oscillations in the LGN to a lesser degree (Lorincz et al., 2009). However, feedback from V1 appears to play an important role at higher frequencies. For instance, interareal synchrony in the beta frequency range can help route information during selective attention (Buschman and Miller, 2007; Saalmann et al., 2007). Accordingly, feedback from V1 has been reported to modulate beta oscillatory activity in the LGN according to attentional demands (Bekisz and Wróbel, 1993).

In summary, there is growing evidence from human fMRI and macaque physiology studies that the response magnitude of LGN neurons is influenced by perceptual and cognitive tasks. Thus, the LGN may regulate information transmission from the retina to visual cortex according to behavioral context. Although the spike timing of LGN neurons is important in influencing thalamo-cortical transmission, perceptual and cognitive modulation of spike timing in the LGN of awake, behaving primates has been largely unexplored.

Pulvinar: Modulation of Information Transmission between Cortical Areas?

Despite being the largest nucleus in the primate thalamus, the pulvinar has been studied much less than the LGN. In the 1970s, evidence started emerging for visual functions of the pulvinar, based on RF properties of its neurons and connections with visual cortex (Allman et al., 1972; Benevento and Rezak, 1976; Mathers and Rapisardi, 1973). These findings were extended in the 1980s by monkey physiology studies demonstrating modulatory effects of attention and eye movements on responses of pulvinar neurons (Bender, 1982; Petersen et al., 1985; Robinson et al., 1986). These data, and the effects of pulvinar lesions (Chalupa et al., 1976; Ungerleider and Christensen, 1977), suggested a role for the pulvinar in visual attention. However, few experiments followed up on these initial promising results, and the pulvinar remains relatively poorly understood and understudied brain territory. We will review both the older literature and the more recent studies that have begun to characterize a novel and possibly fundamental functional role of the pulvinar in regulating cortico-cortical communication.

Anatomy and Physiology

Traditionally, the pulvinar has been divided into medial, lateral, inferior, and anterior areas. However, these cytoarchitectonically defined divisions do not correspond well with divisions based on connectivity, neurochemistry, or electrophysiological properties (Adams et al., 2000; Gutierrez et al., 1995; Stepniewska and Kaas, 1997). Based on retinotopic organization and cortical connections, at least four visual areas of the pulvinar have been differentiated. There are two areas with clearly organized retinotopic maps in the lateral and inferior parts of the pulvinar, which connect with ventral visual cortex. The other two pulvinar areas do not show clear retinotopy: an inferomedial area that connects with dorsal visual cortex (areas MT, MST and FST), and a dorsal area that connects with the posterior parietal cortex (PPC) and frontal eye fields (Figure 1B). The RF size of pulvinar neurons appears to roughly correspond to that of cortical neurons to which they connect (Bender, 1982; Petersen et al., 1985). The majority of pulvinar neurons respond phasically to the onset of visual stimuli, although a number of pulvinar neurons show more tonic responses (Petersen et al., 1985). Pulvinar neurons have been reported to show broad orientation tuning and weak directional preference for moving stimuli, and a subset of neurons show color-sensitivity, including color-opponent responses (Bender, 1982; Felsten et al., 1983; Petersen et al., 1985).

The pulvinar is heavily connected to the cortex and forms cortico-thalamo-cortical pathways. As a general principle, directly connected cortical areas will be indirectly connected via the pulvinar (Figure 1C; Sherman and Guillery, 2006; Shipp, 2003). The direct cortico-cortical feedforward connections originate in layer 3 and terminate in layer 4 in a higher cortical area (Felleman and Van Essen, 1991). In parallel, the putative feedforward pathways through the pulvinar originate in cortical layer 5 and terminate in layer 4 of the higher cortical area as well. There are also direct and indirect feedback pathways between cortical areas. The direct cortico-cortical feedback connections commonly project from layer 6 to layer 1 of the lower cortical area. Cortical layer 6 also provides feedback to the pulvinar, which itself projects to cortical layer 1 (Benevento and Rezak, 1976; Lund et al., 1975; Shipp, 2003). The fact that the direct and indirect pathways terminate in similar cortical layers presents an opportunity for the two pathways to interact.

Apart from cortico-pulvino-cortical pathways, there is a pathway that connects the superficial layers of the superior colliculus (SC) to dorsal visual cortex (MT, V3) through the inferior pulvinar (Berman and Wurtz, 2010; Glendenning et al., 1975; Lyon et al., 2010). Because the superficial SC layers receive retinal input, this pathway probably represents a second route from the retina to visual cortex that bypasses the LGN. The fast transmission time estimated between the SC and MT (Berman and Wurtz, 2010) suggests that this pulvinar pathway may be well suited to mediate motion detection, saliency processing, and saccadic suppression. In addition, the pulvinar, like the LGN, receives modulatory subcortical input from the TRN and cholinergic brainstem sources (Fitzgibbon et al., 1995; Fitzpatrick et al., 1989). Interestingly, the subthalamic nucleus zona incerta provides inhibitory input to the pulvinar, but not the LGN (Power et al., 1999). Because brainstem cholinergic inputs suppress zona incerta activity (Trageser et al., 2006), increased vigilance may result in disinhibition of pulvinar neurons, including the facilitation of transmission along the colliculo-cortical pathway (Trageser and Keller, 2004). Due to the overall connectivity pattern, the pulvinar is positioned to regulate cortico-cortical transmission according to behavioral context.

Effects of Pulvinar Lesions

Arguably the most compelling evidence for the pulvinar playing an important role in visual perception and behavior comes from lesion studies in humans and monkeys. Cortical lesions involving the posterior parietal cortex (PPC) may lead to profound attentional deficits such as visuo-spatial hemineglect, a syndrome associated with a failure to direct attention to contralesional space. Neglect not only is associated with cortical lesions, but can also occur after thalamic lesions that include the pulvinar (Karnath et al., 2002; Petersen et al., 1987). More specifically, the PPC is interconnected with the dorsal pulvinar

and, accordingly, inactivation of the dorsal pulvinar in monkeys leads to deficits in directing attention to contralateral space (Wilke et al., 2010). Even though thalamic neglect in humans is rare and severe attentional deficits that occur as a consequence of pulvinar lesions typically do not persist, a milder deficit that may be a residual form of thalamic neglect has been observed as a slowing of orienting responses to contralesional space (Danziger et al., 2001–2002; Rafal and Posner, 1987).

More generally, patients with pulvinar lesions present with deficits in coding spatial information in the contralesional visual field. They have difficulty localizing stimuli in the affected visual space and these difficulties extend to the binding of visual features based on spatial information (Ward et al., 2002), which is one of the most fundamental operations that the visual system has to perform in order to integrate visual information across various feature dimensions. For example, these patients may have difficulties binding the appropriate color to each of multiple shapes that are presented simultaneously: a red square and a blue circle may be mistaken to be a blue square or red circle. Such errors in binding information from different feature dimensions that require accurate spatial coding are classically associated with PPC lesions (Friedman-Hill et al., 1995) but appear to be associated with pulvinar lesions as well (Arend et al., 2008; Ward et al., 2002). Interestingly, the spatial coding deficits have been observed in different spatial reference frames (e.g., retinotopic or object-based), thus underlining the close functional relationship between the (dorsal) pulvinar and PPC (Ward and Arend, 2007).

In accordance with its role in visual attention, patients with pulvinar lesions also show deficits in filtering distracter information. While these patients have no difficulty discriminating target stimuli when shown alone, discrimination performance is impaired when salient distracters are present that compete with the target for attentional resources, consistent with a difficulty in filtering out the unwanted information present in the visual display (Danziger et al., 2004; Snow et al., 2009). Similar filtering deficits have been observed after PPC lesions in humans (Friedman-Hill et al., 2003) and after extrastriate cortex lesions that include area V4 in humans (Gallant et al., 2000) and monkeys (De Weerd et al., 1999), suggesting that the pulvinar is part of a distributed network of brain areas that subserves visuo-spatial attention.

In monkeys, dorsal pulvinar lesions have also been shown to affect visually guided behavior such as reaching and grasping contralesional targets (Wilke et al., 2010), similar to the optic ataxia produced after lesions to superior parietal areas that process motor intentions and represent peripersonal space (e.g., Battaglia-Mayer and Caminiti, 2002).

Taken together, lesion studies point to the critical involvement of the pulvinar in a number of fundamental cognitive functions, including orienting responses and the exploration of visual space, spatial coding of visual information necessary for feature binding, the filtering of unwanted information, and visually guided behavior. These studies indicate that the pulvinar is an integral subcortical part of multiple large-scale networks that regulate behavior.

Behavioral Response Modulation

The findings from lesion studies are corroborated by physiology and neuroimaging studies showing that neural responses in the pulvinar reflect the behavioral relevance of stimuli. In human neuroimaging studies, modulation of responses has been shown in several different parts of the human pulvinar, including dorsomedial and inferior regions, using selective attention tasks that emphasized directing attention to a spatial location (Kastner et al., 2004), filtering of unwanted information (LaBerge and Buchsbaum, 1990), and shifts of attention across the visual field (Yantis et al., 2002). In monkey physiology studies, it has been demonstrated that spatial attention modulates the response magnitude of neurons in dorsal, lateral, and inferior parts of the pulvinar (Bender and Youakim, 2001; Petersen et al., 1985). Neural responses typically increased by up to 25% or more and, in some cases, spontaneous activity was also affected. In addition to response magnitude, the timing and variability of pulvinar responses is likely to influence information transmission to the cortex. Accordingly, pulvinar neurons show reduced response variability during peripheral attention and saccade tasks (Petersen et al., 1985).

Like other thalamic cells, pulvinar neurons are able to respond in burst or tonic firing modes. Because the activity of the low-threshold calcium channel depends on cell membrane potential, modulatory inputs to the pulvinar may influence the firing mode. Cholinergic inputs will probably depolarize most pulvinar neurons, switching their firing from burst to tonic mode (Varela and Sherman, 2007). However, unlike the LGN, muscarinic activation hyperpolarized about one-fifth of rat pulvinar neurons, suggesting that cholinergic inputs can induce bursting in these neurons (Varela and Sherman, 2007). In addition, inhibitory input to the pulvinar from sources such as the TRN, the anterior pretectal nucleus, and the zona incerta (Bokor et al., 2005; Power et al., 1999) may sufficiently hyperpolarize pulvinar neurons, to enable burst firing. Although data on the relationship between pulvinar burst firing mode and behavior is lacking, it has been shown that pulvinar neurons are more frequently in burst firing mode than LGN neurons (Ramcharan et al., 2005), and thus burst firing may play a larger role in cortico-cortical transmission than retino-cortical transmission.

Regulation of Cortico-Cortical Transmission

The direct cortico-cortical pathways are commonly thought to be the major routes for the transmission of visual information between cortical areas (but see, e.g., Sherman and Guillery, 2006). Given that these direct pathways are paralleled by indirect pathways through the pulvinar, it is important to ask what function these cortico-thalamo-cortical pathways may serve. In vitro studies have shown that microstimulation of the indirect pathways strongly activated cortical areas (Theyel et al., 2010). Moreover, inactivation of the thalamic projection zone that two interconnected cortical areas share led to a failure of cortico-cortical communication, raising the possibility that all cortico-cortical information transmission may strongly depend on thalamic loops (Theyel et al., 2010).

How does pulvinar output influence cortical activity? Simultaneous recordings of LFPs from the lateral posterior-pulvinar complex and visual cortex of cats performing a spatial discrimination task have demonstrated interareal synchrony of beta-band oscillations when the animal anticipated the visual target (Figure 6; Wróbel et al., 2007). In anesthetized cats, deactivating the pulvinar has been reported to disrupt oscillatory activity in

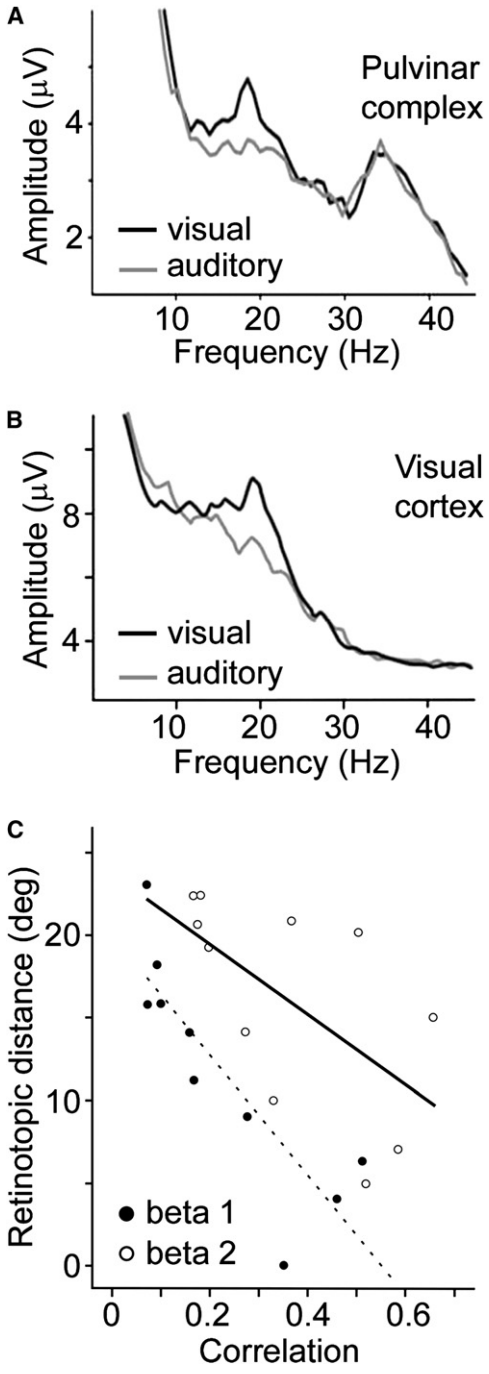

Figure 6. Synchrony between the Pulvinar Complex and Visual Cortex

(A and B) Power in the beta frequency range of the local field potential (LFP) increased in the (A) lateral posterior-pulvinar complex and (B) visual cortex (area 18) when cats performed a spatial discrimination task based on visual rather than auditory cues.

(C) Synchrony between the lateral posterior-pulvinar complex and visual cortex was measured as the phase correlation between LFPs at the respective recording sites. Thalamo-cortical synchrony in the beta frequency range increased with increasing similarity of the visual field representations at the recording sites (displayed as retinotopic distance).

Beta 1 = 12–19 Hz; Beta 2 = 17–25 Hz. Adapted with permission from Figures 2, 4, and 7 in Wróbel et al. (2007).

visual cortex (Molotchnikoff and Shumikhina, 1996; Shumikhina and Molotchnikoff, 1999). Together, these results suggest that the pulvinar may facilitate oscillatory activity in visual cortical areas. Such oscillatory activity may be controlled by thalamo-cortical cells that synapse on fast-spiking (FS) inhibitory cortical neurons (Cruikshank et al., 2007; Gibson et al., 1999; Puig et al., 2008). FS neurons are known to be involved in generating oscillatory activity—that is, alternating inhibition and excitation between FS and pyramidal neurons. Thalamo-cortical inputs may initially activate a group of FS cells, setting up oscillatory activity in the gamma range (>30 Hz) for instance, which is then maintained by means of local cortical mechanisms such as recruitment of additional FS cells through chemical and electrical couplings (Puig et al., 2008).

What may be the functional role of such oscillatory activity in cortico-thalamo-cortical communication? As previously mentioned, oscillations are able to gate input to an area, by restricting effective information transmission to times of reduced inhibition. It has been proposed that the pulvinar may synchronize oscillations between interconnected cortical areas (Jones, 2001; Saalmann and Kastner, 2009; Shipp, 2003), thereby modulating the efficacy of cortico-cortical information transfer. Initial support for such a proposal comes from pulvinar deactivation studies that have shown disrupted synchrony between two sites in area 17 or 18 of anesthetized cats (Shumikhina and Molotchnikoff, 1999). However, it is not clear how the cognitive or perceptual state might affect pulvinar influence on cortico-cortical transmission. A necessary test of the hypothesis that the pulvinar synchronizes cortical areas according to behavioral context requires simultaneous recordings from at least two interconnected cortical areas and the corresponding projection zone in the pulvinar in awake, behaving animals. In recent studies, we have simultaneously recorded from the pulvinar, V4, TEO, and LIP of macaque monkeys performing a spatial attention task (Saalmann, Y.B., Pinsk, M.A., Li, X., and Kastner, S. 2010. Soc. Neurosci. abstract 413.10). Recording electrodes targeted pulvinar sites interconnected with the cortical areas, as determined by probabilistic tractography on diffusion tensor imaging data. Our preliminary findings suggest that the pulvinar causally influenced the cortex in the beta frequency range during selective attention and, accordingly, synchrony between the cortical areas increased at the same frequencies. Thus, the pulvinar may be able to regulate information transfer between cortical areas based on attentional demands. Because direct and indirect feedforward pathways project to cortical layer 4 and direct and indirect feedback pathways project to cortical layer 1 (Figure 1C), the pulvinar is well positioned to regulate both feedforward and feedback cortical pathways. Together, these results provide first evidence for an important role of the pulvinar in regulating cortico-cortical information transmission through the modulation of interareal synchrony during cognitive tasks.

In summary, lesion studies have shown that the pulvinar is critically involved in visual perception, attention, and visually guided behavior. However, it is unclear how the different subdivisions of the pulvinar contribute to these functions. Although anatomical studies have revealed basic principles of pulvino-cortical connectivity, little is known about the physiological interactions of the pulvinar and cortex. First evidence suggests a fundamental role

of the pulvinar in increasing the efficacy of cortico-cortical information transmission. Studies of pulvino-cortical networks probing visual and cognitive behavior that use human neuroimaging and simultaneous neural recordings from macaque thalamus and cortex will be needed to characterize this functional role further.

TRN: Modulator and Pacemaker of Thalamo-Cortical Signals?

Early accounts suggested that the TRN exerted spatially nonspecific influences, largely due to its connectivity with more than one thalamic nucleus, diffuse input from the brainstem, and the extensive dendrites of TRN neurons (reviewed in Guillery and Harting, 2003). However, through the 1970s and 1980s, it became apparent that the TRN and its connections with thalamic nuclei are topographically organized (Crabtree and Killackey, 1989; Montero et al., 1977), suggesting relatively targeted and specific influences on thalamo-cortical cells. These findings were consistent with theoretical accounts proposing a role of the TRN in selective attention by gating thalamic signals (Crick, 1984; Guillery et al., 1998; Yingling and Skinner, 1976). However, compelling evidence in support of this hypothesis emerged only recently from monkey physiology studies (McAlonan et al., 2006, 2008), which we will review in this section as well as the mechanisms by which the TRN may control thalamo-cortical transmission.

Anatomy and Physiology

The TRN is subdivided into sectors, each associated with a different thalamo-cortical pathway. The visual sector of the TRN receives cortical input from layer 6 as well as thalamic input from the LGN and pulvinar in the form of collaterals from descending or ascending fibers. However, the TRN only projects to the thalamus, providing inhibitory input to the LGN and pulvinar. The TRN contains topographically organized representations of the visual field, with the RF size of many TRN neurons comparable to that of LGN neurons (McAlonan et al., 2006). The TRN input to the LGN is retinotopically organized (Crabtree and Killackey, 1989; Montero et al., 1977), suggesting that the TRN can influence thalamic processing at specific locations in the visual field. However, the TRN is unlikely to selectively modulate magno-, parvo-, or koniocellular pathways, because an individual TRN axon projects to multiple LGN layers (Uhlrich et al., 2003). In contrast with the high spatial specificity of the TRN's input to the LGN, the TRN input to the pulvinar appears to be only roughly topographically organized (Fitzgibbon et al., 1995). Tracer studies have shown that there are reciprocal connections between the TRN and the LGN or pulvinar, forming closed loops. Nonetheless, incomplete overlap in thalamic labeling after the injection of retrograde and anterograde tracers into the TRN suggests that a number of TRN neurons synapse on thalamo-cortical neurons that do not project back to the same TRN neurons, consequently forming open loops (Fitzgibbon et al., 1995; Pinault and Deschênes, 1998). Such open and closed loops offer lateral and feedback inhibition, respectively. In addition to these loops formed between the TRN and an individual thalamic nucleus, there are pathways between different thalamic nuclei via the TRN. These disynaptic, intrathalamic pathways can connect first-order and higher-order thalamic nuclei within the same modality, or connect two nuclei of different modalities. These pathways inhibit the target nucleus, thereby providing a means to facilitate information transmission through one thalamic nucleus, while suppressing another one (Crabtree et al., 1998; Crabtree and Isaac, 2002).

TRN neurons respond transiently and with short latency to visual stimuli (McAlonan et al., 2006), suggesting that the TRN can influence early evoked responses of LGN and pulvinar neurons. TRN neurons also have high spontaneous activity (McAlonan et al., 2006), consistent with a tonic inhibition of thalamic nuclei. There is growing evidence for modulation of TRN responses depending on stimulus context. For example, in anesthetized rats, TRN neurons have been reported to habituate to repetitive stimuli (Yu et al., 2009a) and to increase their response to deviant stimuli in an oddball paradigm (Yu et al., 2009b). The TRN receives input from the prefrontal cortex, visual cortex, SC, and cholinergic brainstem nuclei (Kolmac and Mitrofanis, 1998; Montero, 2000; Zikopoulos and Barbas, 2006), which may enable the TRN to integrate information from various processing levels and to modulate its output according to behavioral needs.

Attentional Modulation

The TRN has been implicated in playing an important role in selective attention by regulating thalamo-cortical information transmission (e.g., Crick, 1984; Guillery et al., 1998; Yingling and Skinner, 1976). The effects of TRN lesions are consistent with such a role. For example, like in humans, the reaction times of rats to visual targets that are cued are faster than those to targets that are not. However, a unilateral TRN lesion has been shown to abolish this behavioral advantage for the cued stimulus, suggesting that the TRN normally contributes to directing attention to a cued location (Weese et al., 1999). Rat TRN lesions have also been reported to impair orienting responses and, more generally, to reduce exploratory behavior (Friedberg and Ross, 1993).

There is converging evidence from metabolic mapping and electrophysiology studies that selective attention modulates the activity of TRN neurons. Increased activity, as gauged by the number of Fos-labeled cells, has been observed in the visual sector of the rat TRN for attended visual stimuli relative to unattended stimuli (McAlonan et al., 2000). Moreover, increased deoxyglucose uptake has been demonstrated in the TRN of macaques performing a feature-based attention task (Vanduffel et al., 2000). Single-neuron recordings in macaques using cues to guide their attention directly show specific modulatory effects of attention on TRN neuronal responses. When visual and auditory stimuli were simultaneously presented, the spike rate of neurons in the visual sector of the TRN increased when monkeys directed attention to the visual stimulus relative to when they attended to the auditory stimulus (McAlonan et al., 2006). When a monkey attended to one of two visual stimuli presented simultaneously, the spike rate of TRN neurons decreased relative to that evoked by the same stimulus when unattended (Figure 3C; McAlonan et al., 2008). Although magnocellular LGN neurons tended to have a slightly shorter response latency to the visual stimuli, the attentional modulation started in the TRN before LGN, suggesting that the TRN contributed to the attention effects on the LGN. Interestingly, the attentional modulation of TRN responses in the intramodal attention task differed in sign

relative to that found in the cross-modal attention task. The implications of these modulatory effects on thalamo-cortical neurons will be further discussed below.

Response Modes and Oscillatory Activity

Like LGN and pulvinar neurons, TRN neurons fire in burst or tonic modes depending on the level of vigilance. Importantly, the firing mode can significantly influence the TRN response to sensory stimulation. TRN neurons reach their peak response rate more rapidly for sensory stimulation during tonic mode relative to burst mode. Considering the corresponding time courses of inhibition exerted on thalamo-cortical neurons, tonic mode may thereby facilitate rapid changes in thalamo-cortical signaling, while burst mode may permit an initially strong evoked response from thalamo-cortical neurons (Hartings et al., 2003).

TRN neurons are critically involved in initiating and sustaining thalamo-cortical oscillations. For example, a deafferented TRN is able to self-generate oscillations in the 7–15 Hz range (spindles; Steriade et al., 1987). Moreover, interactions between TRN and thalamo-cortical neurons sustain oscillations—that is, TRN neurons inhibit thalamo-cortical neurons, which rebound fire to excite TRN neurons, thereby initiating another oscillatory cycle (Steriade et al., 1993). In addition to its prominent role in spindle generation, the TRN has been shown to oscillate at lower (Amzica et al., 1992) and higher frequencies, including the beta/gamma frequency range (Pinault and Deschênes, 1992). These different oscillation frequencies manifest during different behavioral contexts. Spindles and lower frequencies commonly occur during states of low vigilance, while beta/gamma frequencies are more associated with increased vigilance (Steriade et al., 1993). It appears that spindle oscillations may contribute to reduced efficacy of information transfer across retino-thalamic synapses, by decorrelating retinal input from thalamic output (Le Masson et al., 2002). A more specific role of response modes and oscillatory TRN activity in cognitive and perceptual tasks remains to be defined.

Influences on Thalamo-Cortical Transmission

TRN neurons may influence thalamo-cortical neurons of the LGN and pulvinar in a number of ways. First, TRN neurons reduce the spike rate of thalamo-cortical neurons through direct inhibition. For example, the responses of TRN neurons evoked by stimuli at unattended locations were shown to increase, while the responses of LGN neurons decreased (McAlonan et al., 2008), thus suppressing thalamo-cortical transmission of information at unattended locations. In the case of an attended visual stimulus, the converse response pattern was found—that is, responses of LGN neurons increased, while the responses of TRN neurons decreased, thus facilitating the transmission of information at attended locations. Such an inverse correlation has also been reported in anesthetized cats between simultaneously recorded neurons in the LGN and the perigeniculate nucleus, the equivalent of the TRN's visual sector in the cat (Funke and Eysel, 1998).

Second, it is possible that TRN neurons increase the responses of thalamo-cortical neurons through disinhibition. Disinhibition of thalamo-cortical neurons has been shown to arise from TRN neurons inhibiting other TRN cells via dendrodendritic synapses (Pinault et al., 1997) or from TRN neurons synapsing on local inhibitory thalamic neurons, which constitutes about 10% of the synapses formed by TRN neurons projecting to the dorsal thalamus of the cat (Liu et al., 1995; Steriade et al., 1986). Such disinhibitory mechanisms may facilitate the thalamo-cortical transmission of relevant information (Steriade, 1999).

Third, TRN neurons may contribute to switching the firing mode of thalamo-cortical neurons. Direct TRN input hyperpolarizes thalamo-cortical cells, which typically invokes burst firing (Huguenard, 1996). Consequently, modulation of TRN activity may change the firing mode of thalamo-cortical neurons and the way information is transmitted to cortex (Yu et al., 2009b).

Finally, the TRN may impact the synchrony and oscillatory patterns of thalamic neurons. TRN inhibitory input to LGN and pulvinar neurons may constrain their spike times to time windows following periods of inhibition, thereby helping to synchronize thalamic output (Steriade et al., 1996). Furthermore, it has been argued that the TRN might function as a pacemaker of thalamo-cortical oscillations (Fuentealba and Steriade, 2005). For thalamo-cortical synchrony at spindle frequencies, cortical feedback appears to drive TRN-mediated inhibition and rebound firing of thalamic neurons. Thus, these neurons are recruited into thalamo-cortical spindle oscillations during states of low vigilance (Destexhe et al., 1998). In contrast, thalamo-cortical synchrony at higher frequencies, in the beta/gamma band, may rely more on direct cortical feedback providing excitatory input to thalamo-cortical neurons. In this case, the role of the TRN neurons may be to influence thalamo-cortical beta/gamma oscillations by resetting their phase (Pedroarena and Llinás, 1997). Such a phase reset may help to synchronize localized beta/gamma oscillations between the thalamus and cortex, thereby increasing information exchange during states of increased vigilance. This is consistent with the localized enhancement of gamma oscillations in sensory cortex that has been reported after electrical stimulation of the TRN (Macdonald et al., 1998). Such an account is also supported by a recent computational model showing that the TRN, via other thalamic nuclei, is well positioned to help synchronize areas of the cortex (Drover et al., 2010). However, a functional role of such TRN influences on thalamo-cortical synchrony and oscillations in perception and cognition remains to be determined.

In summary, the TRN forms cortico-reticular-thalamic loops that allow the TRN to influence both the LGN and pulvinar, and this may include playing the role of a pacemaker coordinating the visual thalamus. Although the empirical evidence is sparse, the TRN has a rich mechanistic infrastructure to flexibly control both thalamo-cortical and cortico-thalamic signal transmission according to behavioral context.

Conclusion

The overall evidence that has emerged during recent years suggests that the visual thalamus serves a fundamental function in regulating information transmission to the cortex and between cortical areas according to behavioral context. Selective attention and visual awareness have been shown to modulate LGN activity, thus indicating that the LGN filters visual information before it reaches the cortex. Behavioral context appears to even more strongly modulate pulvinar activity and, due to its connectivity, the pulvinar is well positioned to influence feedforward and feedback information transmission between cortical

areas. Because the TRN provides strong inhibitory input to both the LGN and pulvinar, the TRN may control and coordinate the information transmitted along both retino-cortical and cortico-cortical pathways.

The visual thalamus serves as a useful model for the thalamus in general because of common cellular mechanisms and thalamo-cortical connectivity principles across different sensorimotor domains. Specifically, the LGN and pulvinar respectively serve as models for first- and higher-order thalamic nuclei, under inhibitory control from associated sectors of the TRN. Because the pulvinar receives input from the SC to form an extra-geniculate pathway to cortex, the pulvinar also promises to be a useful model for higher-order thalamic nuclei that receive ascending sensory information from brainstem inputs—that is, nuclei exhibiting mixed first- and higher-order characteristics.

As noted in our review, there are bold question marks regarding the exact role of the visual thalamus, particularly the pulvinar and TRN, in perception and cognition, and our account of these functional roles cannot be more than an approximation based on sparse experimental evidence at this time. While there has been much study in in vitro and in anesthetized in vivo preparations of the cellular mechanisms involved in thalamo-cortical transmission, studies are missing that will link the mechanistic details to perceptual and cognitive operations. For example, it is still not clear how firing modes or oscillatory activity in the thalamus relate to perceptual and cognitive processing. Basic electrophysiology studies of the thalamus in animals performing perceptual and cognitive tasks are much needed. Moreover, although selective attention has been shown to modulate neural activity in the LGN, pulvinar, and TRN, it is not clear how the TRN interacts with the LGN and pulvinar, nor how the thalamus interacts with cortex depending on behavioral context. These network properties will need investigation using simultaneous recordings from thalamic and cortical areas in awake, behaving primates.

One reason for the scarcity of studies on the visual thalamus in awake, behaving animals may be the classical view that cognition is the exclusive domain of the cortex. An additional reason is presumably methodological, such as the difficulty in targeting thalamic regions. However, this problem has been greatly reduced since structural imaging of macaque brains has become routine. Moreover, combining electrophysiology with electrical stimulation (Berman and Wurtz, 2010) or diffusion tensor imaging (Saalmann, Y.B., Pinsk, M.A., Li, X., and Kastner, S. 2010. Soc. Neurosci. abstract 413.10) allows subregions of thalamic nuclei to be targeted based on connectivity.

Although there are still many unanswered questions about the role of the thalamus in perception and cognition, converging evidence from neuroimaging, physiological, anatomical, and computational studies suggests that the classical view of cognitive functions exclusively depending on the cortex needs to be thoroughly revised. Only with detailed knowledge of thalamic processing and thalamo-cortical interactions will it be possible to fully understand cognition.

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